

**AMENDMENT UNDER 37 C.F.R. § 1.114(c)**  
**U.S. Application No. 10/532,605 (Q87625)**

**REMARKS**

**Status of Claims and Amendment**

Claims 6 and 9 have been amended. Claims 10, 21, 23, 25, 27, 29, 35, 37, 39, and 41 have been canceled. Claims 1-5, 7-8, and 12-16 were previously canceled. Claims 6, 9, 11, 17-20, 22, 24, 26, 28, 30-34, 36, 38, 40, and 42 are all the claims pending in the application.

Claims 6 and 9 have been amended to incorporate the limitations of claim 10.

No new matter is added.

**Response to Advisory Action mailed April 30, 2009**

In the Advisory Action, the Examiner indicated that the request for reconsideration has been considered, but does not place the application in condition for allowance because it appears the Examiner has found Applicants' arguments that Olsen does not disclose the presently claimed enzyme not to be persuasive.

Specifically, the Examiner asserted that Applicants contradict their argument by the disclosure in their own specification disclosing that "it was confirmed that the amino acid sequence of the purified enzyme obtained in Example 1 is completely identical to the subtilisin DY" (page 33, 2<sup>nd</sup> paragraph of specification), and that "subtilisins may be used in the present invention, and subtilisin DY (WO/30682) is preferable" (page 16, last paragraph of specification). The Examiner appears to have asserted that since WO 98/30682 (Olsen) teaches the claimed enzyme, the properties of the claimed enzyme would be inherent to the enzyme disclosed by Olsen.

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The Examiner also appears to have asserted that one of ordinary skill in the art at the time the invention was made would have known that the mobility of a protein in an SDS-PAGE gel would depend on the percentage of acrylamide used so that the molecular weight of a protein shown on such a gel would vary based upon the percentage of acrylamide used. The Examiner pointed to page 29, 2<sup>nd</sup> and 3<sup>rd</sup> paragraphs of the present specification, which discloses that “an SDS-PAGE using a 12% gel ...and the molecular weight of the enzyme capable of digesting a pathogenic prion protein was approximately 31,000, ... another SDS-PAGE using a 15 % gel was carried out ... and the molecular weight of the enzyme capable of digesting a pathogenic prion protein was approximately 26,000” in support of this position.

In response to Applicants’ arguments that the Examiner has failed to provide reasons why one of skill in the art would combine the cited references to arrive at the claimed method of using the claimed enzyme, the Examiner asserted that Shih teaches a method for digesting infectious prion proteins comprising the step of bringing the protein into contact with an enzyme derived from *Bacillus licheniformis*, without preheating the subject at 90°C. The Examiner further asserted that Shih teaches that any protease may be used including keratinase enzymes, subtilisins, and active fragments of a keratinase enzyme. Thus, according to the Examiner, a person of ordinary skill in the art at the time the invention was made would have been motivated to substitute the enzyme described in Shih with the enzyme described in Olsen, to obtain the claimed invention. The Examiner asserted that because the substitution is of one known proteolytic enzyme with another known proteolytic enzyme, i.e., subtilisin DY, such a substitution would have yielded predictable results.

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In response, Applicants note that contrary to the Examiner's contentions, the method of Shih requires a pretreatment step to "cook" the tissue at a temperature from about 100°C to about 150°C (see paragraph [0017] of Shih). Thus, even if the enzyme disclosed in Olsen is, *arguendo*, the same as the claimed enzyme, and one of ordinary skill in the art was somehow motivated to make such a combination, the combination would not result in the claimed method because Shih requires preheating the tissue. Also, because Olsen is merely cited for teaching subtilisin DY, Olsen does not cure the deficiency of Shih.

Thus, the Examiner's rationale for maintaining the present rejection appears to be based upon impermissible hindsight gleaned from Applicants' disclosure, and not from the conclusion that one of ordinary skill in the art would have reached based upon the disclosures of Shih and Olsen, either alone or in combination. M.P.E.P. § 2142. In fact, Olsen was published on July 16, 1998, approximately 2 ¾ years before the Shih application was filed, and there is nothing in either Olsen or Shih teaching or suggesting the presently claimed method, in which the tissue is not preheated prior to enzyme digestion.

Further, even if the tissue in the method of Shih is not subjected to preheating prior to enzyme digestion, Applicants have shown in Example 8 and Figure 6 of the present application, that under such conditions, the claimed enzyme provides unexpectedly superior enzyme digestion of prion proteins in comparison to the keratinase derived from *Bacillus licheniformis* PWD-1 as described in Shih. In this regard, Applicants have shown by comparison

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to the closest prior art, Shih<sup>1</sup>, that the presently claimed method results in unexpectedly superior enzyme digestion without preheating a subject tissue; this could not have been predicted based upon the teachings of Shih and Olsen, either alone or in combination<sup>2</sup>. Such unexpected properties are evidence of the non-obviousness of the claimed invention, and must be considered by the Examiner.

Nevertheless, and solely to advance prosecution of the present application, claims 6 and 9 have been amended to incorporate subject matter from of claim 10.

Reconsideration and withdrawal of the rejection under § 103(a) is respectfully requested.

**Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

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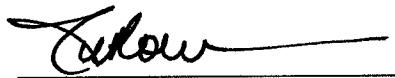
<sup>1</sup> Although evidence of unexpected results must compare the claimed invention with the closest prior art, Applicant are not required to compare the claimed invention with subject matter that does not exist in the prior art. *In re Geiger*, 815 F.2d 686, 689 (Fed. Cir. 1987) (Evidence rebutted *prima facie* case by comparing claimed invention with the most relevant prior art. The Court held the Office failed to establish a *prima facie* case of obviousness.); *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966) (Requiring applicant to compare claimed invention with polymer suggested by the combination of references relied upon in the rejection of the claimed invention under 35 U.S.C. 103 “would be requiring comparison of the results of the invention with the results of the invention.” Id. at 422).

<sup>2</sup> The Supreme Court in KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727, 1741 (2007) suggested that the standard for determining whether a patent claiming a combination of prior art elements would have been obvious should focus on “whether the improvement is more than the predictable use of prior art elements according to their established function.” KSR at 1740. Accordingly, a *prima facie* case of obviousness may be rebutted by a showing of unpredicted or unexpected results.

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Respectfully submitted,



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